CHANGES IN CARDIAC ARRHYTHMIAS AND CORONARY ARTERY DISEASE RISK FACTORS IN 60- TO 92-YEAR-OLD MALE ATHLETES AT 20-YEAR FOLLOW-UP

BY

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For

Lourdes Maria Mengelkoch

I love you

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The prevalence of cardiac arrhythmias and coronary artery disease (CAD) risk factors were determined in 19 senior athletes (runners/walkers) at 20-yr follow-up. Electrocardiographic (ECG) recordings during maximal treadmill exercise (GXT) were compared from initial, 10-yr, and 20-yr follow-up (T1,T2,T3), between 1971 & 1992, and from 18 hr Holter monitoring (HM) at T2 and T3. Subjects were age 60- to 92-yr at T3 and had maintained regular aerobic training ≥ 22 yr. Significant age-related changes occurred in low grade arrhythmias (premature atrial contractions, and ventricular arrhythmias, Lown grades 1 and 2) during GXT, while the occurrence of major ECG abnormalities (ventricular conduction defects (VCD), ventricular tachycardia (VT), ST-

segment depression) remained low, or were never present (left ventricular hypertrophy, nonspecific ST-T wave changes, significant Q waves). We observed that VT and VCD were not present in subjects < 60 yr age, and major ECG abnormalities persisted through follow-up in 50% to 100% of those subjects with the ECG abnormalities. The prevalence of arrhythmias did not appear related to training intensity.

The sensitivity of exercise testing to predict acute cardiac events (myocardial infarction, sudden cardiac death) during physical activity, in senior athletes, using ST-segment depression or VT as markers, was poor (0/4=0%), as the cumulative incidence of acute cardiac events during physical activity was 0%. These data suggest that habitual vigorous exercise and competition, in senior athletes, has low risk for acute cardiac events during moderate and strenuous physical activity.

No significant changes were observed in the occurrence of CAD risk factors throughout follow-up. However, trends were found in which hypercholesterolemia decreased, and total cholesterol:HDL ratios > 5, increased. The occurrence of other risk factors (hypertension, family history of cardiovascular disease, abnormal resting ECG) changed by ≤ 11% at T3, and several risk factors (diabetes, obesity, smoking) were never present. These data suggest that habitual moderate to vigorous exercise, in senior athletes, attenuates the increase in CAD risk factors normally associated with aging.

CHAPTER 1
INTRODUCTION

In the late 1960s and early 1970s there was an increased interest in moderate to high intensity exercise in the middle-aged to elderly population. Many questions were being asked concerning the safety of exercise and competition for persons over age 40, with respect to activity-related acute cardiac events (Myocardial Infarction, MI, or Sudden Cardiac Death, SCD), and the relationship between vigorous exercise and coronary artery disease (CAD). When SCD occurs the foremost underlying clinical cause is CAD.[1-3] Studies report the overall risk of activity-related acute cardiac events is low, and lowest in subjects that habitually exercise compared to sedentary individuals.[4-8] However, risk transiently increases during exercise periods compared to non-exercise periods, and is greatest during strenuous exercise.[6,8] Although this relationship seems paradoxical, the cardioprotective effect of physical activity on CAD is well documented, and thought to offset any increased risk of acute cardiac events during physical exertion.[9-15] Yet, little longitudinal data concerning CAD risk, and cardiovascular complications are reported for middle-aged or elderly athletes, who engage in habitual high intensity training, and

competition, and thus may be a population subject to chronic transient high risk.

Risk factors for CAD increase with age,[16-24] but several cross-sectional studies have reported middle-aged athletes and physically active subjects have lower levels of CAD risk factors compared to sedentary subjects of similar age, until age 65.[25-27] These studies suggest that if subjects maintain long-term physical training, the age-related increase in CAD risk factors may be attenuated. Presently, longitudinal training studies have only reported blood pressure and body composition data, and not thoroughly analyzed changes in CAD risk factors.[28-33]

The exercise electrocardiogram (ECG) is commonly used to screen middle-aged apparently healthy men before initiating a vigorous exercise program, and to detect exercise-induced cardiac arrhythmias and clinically silent myocardial ischemia.[34] The appearance of some ECG abnormalities such as left ventricular hypertrophy (LVH), ventricular conduction defects (VCD), and nonspecific ST-T wave changes are associated with increase risk for CAD and SCD.[16] Ventricular tachycardia and ventricular fibrillation (VT,VF) are the primary arrhythmias associated with SCD.[1-3] Significant Q waves are associated with MI and CAD in subjects with or without a known history of MI.[17,35] However, the relevance of other ECG abnormalities is less certain. Siscovick et al.[36] suggest that exercise electrocardiography has poor sensitivity in predicting risk for acute cardiac events,

during moderate and strenuous physical activity, in asymptomatic, hypercholesterolemic, middle-aged men.

Population-based resting ECG studies have shown the occurrence of arrhythmias and ECG abnormalities increase with age.[17,37] Studies involving ECG recordings from Holter monitoring have shown relatively high occurrences of arrhythmias and conduction disturbances in middle-aged subjects.[38-39] When middle-aged athletes and sedentary subjects were compared during Holter monitoring, a similar incidence of ventricular ectopy was observed, but higher incidences of conduction disturbances were reported in athletes.[39] During exercise testing several studies have shown relatively high incidences of silent ST-segment depression,[25,39-40] and rare occurrences of VT,[41] in middle-aged athletes. The clinical significance of these arrhythmias and ECG abnormalities in this population, however, remains undetermined due to the nature of cross-sectionally designed studies. Interpreting the effect of age and physical training on physiologic responses from cross-sectional data is difficult and misleading because data are not collected on the same persons over time, and lifestyle factors such as exercise habits are not taken into account. Thus, longitudinal studies are required to determine the relationship between age, physical training, and physiological changes. Although several longitudinal studies have reported information on physiological changes in middle-aged subjects who have habitually exercised,[29-33,42] only one

study has reported any information on electrocardiographic abnormalities.[42]

Purpose of the Study

The objective of this project is to evaluate the effect of long-term physical training, and competition on changes in the occurrence of cardiac arrhythmias, ECG abnormalities, and CAD risk factors, in middle-aged and elderly (senior) athletes. This prospective study is a 20-year follow-up evaluation of former champion track athletes, age 60- to 92-yr (mean = 71 yr), who have habitually exercised and competed through their middle-aged and elderly years. The present study is designed to specifically investigate the following questions:

1) Does habitual exercise and competition, in senior athletes, alter the occurrence of cardiac arrhythmias and ECG abnormalities, in terms of supraventricular arrhythmias, ventricular arrhythmias, LVH, VCD, ST-T wave abnormalities, and significant Q waves?

2) Does the occurrence of silent ischemic ST-segment depression and/or VT, in senior athletes, during exercise testing, predict increased risk for acute cardiac events during vigorous training and competition?

3) What are the acute cardiac risks associated with long-term vigorous training and competition in senior athletes?

4) Does the prevalence CAD risk factors (hypertension, elevated blood lipids, smoking, obesity, diabetes, abnormal resting ECG, family history of CV disease) change in senior athletes who have habitually exercised?

Hypotheses

Initially all subjects were competitive champion track athletes who maintained regular high intensity training, and participated in high level competition. Subjects were assigned to high intensity (H), moderate intensity (M), or low intensity (L) subgroups based on intensity of training and competition at 20-yr follow-up. Data were analyzed to compare group and subgroup responses over 3 time periods, initial (T1), 10-yr follow-up (T2), and 20-yr follow-up (T3).

When examining test results at T1, T2, and T3:

1) There will be no significant difference in the occurrence of arrhythmias and ECG abnormalities among senior athletes, and no significant difference in the occurrence of arrhythmias and ECG abnormalities among H, M, and L subgroups.

2) There will be no significant difference in the occurrence of CAD risk factors among senior athletes, and no significant difference in the occurrence of CAD risk factors among H, M, and L subgroups.

Delimitations

This study was delimited to the following:

1) 25 male former champion track athletes who were initially evaluated between 1971 and 1976, and had follow-up evaluations between 1981-1982,

2) subjects had maintained regular aerobic training ≥ 22 yr, and

3) at T3 subjects were 60- to 92-yr-old.

Limitations

1) No age matched control subjects were examined.

2) Testing was not performed at the same laboratory at T1, T2, and T3.

3) Electrocardiographic evaluations from maximal treadmill exercise involved different exercise protocols and lead configurations.

4) Two ECG evaluations were made from two maximal treadmill exercise tests at T2 and T3, but only one ECG evaluation was performed at T1.

4) Holter monitoring was not performed at T1.

5) Maximum oxygen uptake (VO_2max) was determined from different exercise protocols at T2 and T3. Maximum oxygen uptake was determined from expired air samples collected in meterological balloons at T1 and T3, and then analyzed for O_2 and CO_2 content by gas analyzers. At T2 an automated system

was used with expired air samples going directly to a mixing chamber and analyzed by O_2 and CO_2 gas analyzers.

6) Some subjects were taking antihypertensive medication or antiarrhythmic medications at T3 which may have altered exercise performance and physiological responses.

7) Subgroup classification of some subjects changed between T2 and T3 due to changes in training intensity and level of competition.

CHAPTER 2
REVIEW OF LITERATURE

The review of the literature is divided into three sections. The first section reviews research on the acute cardiovascular risks of physical activity. The second section reviews research on physical activity and CAD risk factors. The third section reviews research on the clinical significance of various arrhythmias and ECG abnormalities, and their prevalence in healthy sedentary, physically active, and athletic, middle-aged and elderly individuals.

Cardiovascular Risks of Physical Activity

For many years concern and controversy has existed about the acute cardiovascular risks (MI, SCD) of physical activity. In the late 1960s and early 1970s there was an increased interest in moderate to high intensity exercise and competition in middle-aged and elderly athletes, and a formal circuit of Masters (athletes age $\geq$ 40) running competition developed internationally. Concern and questions of safety were naturally raised that such vigorous training and racing demands may expose individuals to greater risk.

When SCD occurs in subjects $\geq$ 30 yr age the primary underlying cause is CAD.[1-3] Myerburg et al.[2] report that CAD

and its consequences are the dominant pathological finding in approximately 80% of SCD victims.

Epidemiological studies have shown that the acute cardiovascular risk during exertion is low. Thompson et al.[7] reported on the incidence of death during jogging in 30- to 64-yr-old men in the state of Rhode Island. They observed one death per 7,620 joggers per year or approximately one death per 396,000 man-hours of jogging. Gibbons et al.[5] followed 2,935 adults engaged in exercise programs at the Copper Clinic, Dallas, TX. Most subjects were sedentary before entering the program and mean age was 37 yr. This study reported no deaths and only two cardiac events in 374,798 person-hours of exercise. Friedwald and Spence[4] reviewed several studies reporting the annual incidence of SCD associated with exertion. These population studies reported a range of 3.5% to 17% of the victims collapsed during or after exertion. Siscovick et al.[6] and Vuori[8] have assessed the overall risk (during and not during vigorous activity) of SCD and the transient risk during vigorous activity. Siscovick et al.[6] report that risk of SCD transiently increases during activity but is lower for men who habitually exercise (5x increase) compared to those with low levels of habitual activity (56x increase). However, the overall risk was 60% lower among men who habitually exercised vigorously compared to those with lowest activity levels. Among Finnish men, Vuori[8] estimated the overall transient risk of SCD during exercise increases 4.5x and is relative to the intensity of

exercise. In nonstrenuous exercise transient risk increased 3.2x, whereas transient risk increased 9.0x during strenuous exercise. These studies unanimously conclude that although there is a transient increase in risk for cardiovascular events during exercise the overall risk is low, and less in an active lifestyle than a sedentary lifestyle. Thus, at the population level, the cardiovascular risks of physical activity are outweighed by the cardiovascular benefits.

Physical Activity and Coronary Artery Disease Risk Factors

Epidemiological research has shown CAD is a multifactorial disease process and this evidence has given rise to the risk factor concept. That is, CAD is a problem involving a variety of predisposing risk factors each of which are an ingredient of a CAD risk profile. Contributions from the Framingham Study, Longshoremen Study, Harvard Alumni Study, Multiple Risk Factor Intervention Trial, Cardiovascular Health Study, and Lipids Research Clinic Mortality Follow-up Study have identified risk factors and quantified the risks associated with them.[12-14,17,22-24,43-45] Presently, risk factors for CAD include smoking, hypertension, elevated serum cholesterol, elevated low density lipoprotein (LDL) cholesterol, low levels of high density lipoprotein (HDL) cholesterol, obesity, diabetes (glucose intolerance), physical inactivity, age, sex, family history of cardiovascular (CV) disease, and abnormal resting

ECG (LVH, VCD, nonspecific ST-T wave changes, significant Q waves). Many of these risk factors are interrelated and it is often difficult to discern the contribution of each individual factor. Increases in the prevalence of most CAD risk factors (hypertension, blood lipids, diabetes, physical inactivity, obesity, abnormal resting ECG) are associated with increased age.[16-24]

The cardioprotective effect of physical activity (occupational and leisure time) on CAD is well documented, though the primary or secondary influence of physical activity remains controversial.[9-15] Recent meta-analysis data of the effect of physical activity on CAD, from more than 40 studies, indicate that CAD is 1.9 times more likely to develop in sedentary persons compared to those who are physically active.[46] From the Harvard Alumni Study, Paffenbarger et al.[14] report that regular physical activity which expends 2,000 Kcal/week lowers CAD mortality and can prolong life 2 years.

Physical activity appears to favorably effect most CAD risk factors. Haskell[47] reports that regular endurance type training requiring an energy expenditure of approximately 1,000 Kcal/week produces favorable lipid plasma changes. Hagberg and Seals[48] report that regular endurance training moderately reduces systolic and diastolic BP in hypertensive individuals. Exercise training on the order of 25-35 km/wk appears to increase glucose tolerance and decrease insulin resistance.[49] Helmrich et al.[50] reports that data from the

University of Pennsylvania Study found physical activity is effective in preventing non-insulin-dependent-diabetes (NIDDM), and that risk for NIDDM decreased by 6% for each 500 Kcal/wk increment in energy expenditure.

Cross-sectional data on CAD risk factors among middle-aged physically active subjects, and master athletes, report lower levels of risk factors (hypertension, blood lipids, physical inactivity, obesity) compared to inactive subjects of similar age, until age 65.[25-27] These studies suggest that if subjects maintain long-term physical training, the prevalence of CAD risk factors may remain low. However, no long-term physical training studies have thoroughly analyzed changes in CAD risk factors, and thus little information is present about the relationship between habitual moderate-high intensity training and CAD risk factors. To date, only changes in blood pressure and body composition have been reported.[28-33]

Significance and Occurrence of Cardiac Arrhythmias and Electrocardiographic Abnormalities

Certain ECG abnormalities are important clinical indicators of pathology or represent disease risk factors. Recent work from the Framingham study includes the following resting ECG abnormalities as important risk factors for CAD and SCD: LVH, VCD, and nonspecific ST-T wave changes.[16] Other than known CAD, these ECG abnormalities were found to have the highest relative risk for SCD. Significant Q waves are

associated with MI, though the event may go unrecognized in many adults.[17,35] Data from the Framingham study found approximately a third of the subjects had unrecognized MI.[35] In the Cardiovascular Health study over 50% of the subjects with significant Q waves had no history of MI.[17] In the Cardiovascular Health study significant Q waves were found to have the strongest association with CAD.[17] The primary arrhythmias associated with SCD are VT and VF.[1-3]

Significant ST-segment depression during exercise testing is considered a positive indicator of myocardial ischemia and CAD. Recent meta-analysis of 147 published reports comparing exercise-induced ST-segment depression with coronary angiography found mean sensitivity = 68% and specificity = 77%.[51] However, Siscovick et al.[36] report that ST-segment depression, during submaximal exercise testing, has poor sensitivity (18%) in predicting risk for acute cardiac events, during moderate and strenuous physical activity, in asymptomatic, hypercholesterolemic, middle-aged men. Presently, no studies have reported the sensitivity of maximal exercise testing for predicting acute cardiac events, during moderate and strenuous physical activity, in middle-aged and elderly athletes who habitually exercise. Juul-Moller et al.[52] report that silent ST-segment depression during 24 hr Holter monitoring in 68-yr-old men accompanied by ventricular arrhythmias ≥ Lown grade 4, represents a 2-fold increase in risk for cardiac events.

Population based resting ECG studies have observed that ECG abnormalities increase with age.[17,37] Furberg et al.[17] report data from the Cardiovascular Health Study involving 5,150 adults ≥ 65 yr. They found that major ECG abnormalities (defined as VCD, LVH, 1° AV block, major Q/QS waves, ST-T wave abnormalities, and atrial fibrillation) were common among elderly (mean=29%), but greater in males, and greater in subjects with CAD or hypertension. Additionally, they report the prevalence of abnormalities in subjects without a history of CAD or hypertension was 3x greater in subjects ≥ age 85 yr compared to those 65- to 69-yr-old. The prevalence of most arrhythmias in the Cardiovascular Health Study was similar to that reported from the Tecumseh population study[37] involving 663 adults ≥ 50-yr-old.

Because ECG abnormalities are usually transient, the chance of detecting them may be limited using resting or exercise electrocardiograms. Holter monitors provide continuous ECG recordings during normal activities and thus may have a greater opportunity to detect transient arrhythmias. However, the major limitation with Holter monitoring is lack of control of the conditions associated with the initiation of the arrhythmia. Hinkle et al.[38] obtained 6 hr Holter monitoring recordings during ordinary activities from 301 middle-aged men (median = 55 yr). They report that conduction disturbances occurred in 93%, supraventricular arrhythmias in 76%, and ventricular arrhythmias in 62% of the subjects. Kennedy et al.[53] reported

6.5-yr follow-up survival data on asymptomatic middle-aged (mean = 46 yr) subjects who had complex ventricular arrhythmias (≥ Lown grade 3) during 24 hr Holter monitoring. This study found fewer deaths than predicted from a standardized mortality ratio and concluded complex ventricular ectopy suggests no increase risk of death in asymptomatic subjects. Only one published report is available which has performed Holter monitoring in middle-age athletes (n = 20).[39] This study reports the occurrence of ventricular ectopy was similar for controls and athletes (90% vs 75%, respectively), though higher incidences of sinus pauses, and AV conduction disturbances were found in athletes.

Of interest are several cross-sectional reports of high incidences (20-25%) of ST-segment depression, in middle-aged physically active subjects, and young and middle-aged athletes, during maximal exercise.[25,39-40,54] Few studies have reported any occurrence of VT in master athletes during maximal exercise.[41-42] Data from the Baltimore Longitudinal Study on Aging indicate the incidence of asymptomatic, nonsustained VT in apparently healthy subjects is low (10 of 922 subjects = 1.1%), and occurs primarily in elderly subjects (9 of 10 subjects ≥ 65 yr).[55] At 2-yr follow-up no subjects had any cardiovascular events and the report concludes the occurrence of exercise-induced VT did not represent any increased risk for cardiovascular events. Preliminary longitudinal data from Pollock et al.[42] suggests that the incidence of ST-segment depression and VT is low in

master athletes, and not significantly different at 10-yr follow-up. However, the significance of silent ST-segment depression and/or asymptomatic, nonsustained VT in master athletes, in terms of increased risk for acute cardiac events, has not been determined.

CHAPTER 3
METHODS

Initial testing was conducted between 1971 and 1976, primarily at two laboratories. Subjects from the West Coast were tested at the University of California, Davis, and those from the Midwest and East Coast at Wake Forest University, Winston-Salem, NC. One subject was tested at the Aerobics Center, Dallas, TX. The same protocols were used in all laboratories. Ten-yr follow-up evaluations were conducted 9.9 ±1.3 yr (mean ±SD) after initial testing. All 10-yr follow-up evaluations were conducted at the University of Wisconsin Medical School (Milwaukee Clinical Campus), Mount Sinai Medical Center, Milwaukee, WI. Twenty-year follow-up evaluations were conducted between 1991 and 1992, 20.0 ±1.3 yr after initial testing. All 20-yr follow-up evaluations were conducted at the University of Florida and Veterans Administration Medical Center, Gainesville, FL.

Evaluations at T3 required three consecutive days of testing. Subjects arrived the day before testing and the entire protocol, risks, hazards, and benefits of the study were explained to the subjects, and then their written informed consent was obtained. Subjects were instructed not to engage in vigorous physical training, abstain from drinking alcohol for 24 hours prior to testing, and to report

to the laboratory at least 12 hours postprandial. The subjects then completed questionnaires concerning demographic information, cardiovascular health, smoking history, and physical training history during the intervening 10 years from T2.

Subjects

At T1 25 male athletes volunteered as subjects. Nineteen of 25 subjects (76%), age 60-92, from the original sample were available at T3. Of the six subjects not tested at T3, three had orthopedic injuries, one had back problems, one had Alzheimer's disease, and one could not be located. Attempts were made to ascertain whether the unlocated person had died. No death certificate was reported for that subject in his last known county or state of residence. Most subjects were professional people from a variety of occupations. At T3 12 of 19 subjects (63%) were retired. At T1 all subjects had maintained regular endurance exercise training during the preceding 2 years (or more), and all subjects were competitive athletes who had placed 1, 2, or 3 in recent national or regional competition, in running or walking events. Eighteen competed in running events and one in walking events. Of the 18 runners, five competed primarily in sprints ($\leq$800m) and 13 in distance events ($\geq$1500m).

At T1 subjects were given an activity questionnaire to obtain information about the type, quantity, and quality of

training they performed during the year prior to testing. In addition, to running or walking activities, information was obtained concerning strength training (resistance exercise program ≥ 2x per wk), stationary cycling (≥ 2-3x per wk, ≥ 20 min/session), and other aerobic activities. At T2 and T3 the same questionnaire was completed and, in addition, an intensive interview was conducted. The purpose of the interview was to document the subject's training intensity and level of competitiveness during the intervening years and verify the accuracy of the information obtained from the questionnaires. Based on the results of the questionnaire and interview at T3, subjects were placed into one of three groups:

High Intensity (H)

Subject's usual training intensity was = 60-85% maximum heart rate (HR) reserve, subject performed ≥ 1/wk an interval session or aerobic threshold training session (≥ 85% maximum HR reserve), and subject continued high level competition.

Moderate Intensity (M)

Subject's usual training intensity was = 60-80% maximum HR reserve, and subject rarely competed.

Low Intensity (L)

Subject changed mode of activity (running to walking), subject's usual training intensity was ≤ 70% maximum HR reserve, and subject did not compete.

Physical Examination and Body Composition Measurements

Subjects reported to the laboratory in the morning after a 12 hr fast. They had refrained from vigorous exercise the previous day. The subjects were given a physical examination which included chest auscultation, and determination of resting HR, and resting blood pressure (BP) after a 15 min quiet sit. A venous blood sample was drawn for analysis of total cholesterol, HDL-cholesterol (not analyzed at T1), and fasting glucose levels (not analyzed at T1). Body composition was determined from height, weight (W), and skinfold fat measurements. Skinfold fat measurements were obtained from seven sites (chest, axilla, triceps, subscapula, abdomen, suprailiac, anterior thigh) using Lange calipers (Cambridge Scientific Industries) following the recommendations described by Pollock and Wilmore.[56] Body density (D_b) was predicted from the equation for males developed by Jackson and Pollock: $D_b = 1.11200000-0.00043499(\Sigma 7)+0.00000055(\Sigma 7)^2-0.00028826(age)$.[57] Percent fat was calculated from the Siri equation: $\%fat = 4.950/D_b - 4.50 * 100$.[58] Fat free mass (FFM) was calculated from %fat using the formula: FFM = W - (W * %fat * 0.01).

Exercise Testing and Holter Monitoring

A standard, resting, supine 12-lead ECG was recorded immediately before exercise. At T1 exercise 12-lead ECG recordings and VO_2max were assessed from a single maximal treadmill exercise test using either a running or walking protocol, depending on the subject's track specialty. A continuous multistage protocol was used in which the speed was held constant and the grade varied. The test began with 3 min at 0% grade, followed by a 2.5% grade increase every 2 min until exhaustion. Speed was dependent on the subject's estimated level of fitness with the test being designed to exhaust him within 8-12 min. At T2 and T3, two maximal treadmill exercise tests were conducted over a 2 day period. Because of the subjects increased age at T2, it was felt that a diagnostic test using the standard Bruce protocol[59] was necessary to screen the subjects for possible ischemia before administering the VO_2max test. On Day 1 (T2 and T3) the standard Bruce protocol was used for exercise 12-lead ECG evaluation. On Day 2 (T2) VO_2max was determined using the original running or walking protocol, as described above, and an exercise 7-lead ECG (I,II,III,aVR,aVL,aVF,V5) recorded. On Day 2 (T3) VO_2max was determined using the standard Bruce protocol and an exercise 12-lead ECG recorded. One exception in exercise protocol was made at T3 for a subject who had orthopedic limitations (total hip replacement). For this

subject the Naughton protocol[60] was used which is a standardized walking protocol.

At T1 and T3, expired air samples were collected in 150 l meteorological balloons or in aliquot bags and analyzed for O_2 and CO_2 content by gas analyzers (O_2: T1 - Beckman E2; T3 - AMETEK S3A1. CO_2: T1 - Beckman LB1; T3 - AMETEK P-61-B). At T2 an automated system was used with expired gas samples going directly to a mixing chamber and analyzed by Beckman O_2 (OM-11) and CO_2 (LB-2) gas analyzers.[61] Gas analyzers were calibrated before and after each test with reference gases using the Haldane method.[62] Expired volume was measured using a Parkinson-Cowan dry gas meter, model CD-4 at T1 and T2. At T3 expired volume was measured with a 120 L Tissot chain-compensated spirometer (Collins) and corrected to STPD conditions for VO_2max calculations.[62]

Following maximal treadmill exercise on Day 1 (T2, T3), continuous ECG recordings of subjects during free activity were obtained using Holter monitors. A 2-channel Holter monitor (T2 - Avionics model 445; T3 - Oxford Medilog 4500) was applied utilizing a bipolar electrode lead system (modified V1 and V5 exploring leads and a ground lead).

Electrocardiographic Analysis

Electrocardiographic recordings from all maximal treadmill exercise tests were assessed for arrhythmic events and ECG abnormalities by a cardiologist. Holter ECG

recordings were analyzed for arrhythmic events and ECG abnormalities using high speed scanners (T2-Avionics Electrocardioscanner; T3-Oxford Medilog Excel Analysis System). Detected arrhythmic events and ECG abnormalities were printed as hard copy and verified by a cardiologist.

Arrhythmias and Electrocardiographic Abnormalities

Supraventricular Arrhythmias

premature atrial contractions (PACs)

supraventricular tachycardia (paroxysmal)

atrial flutter

atrial fibrillation

Ventricular Arrhythmias (VA)

Classification by Lown and Wolf[63]

grade 1 - occasional, ≤ 1/min, isolated premature ventricular contractions (PVCs)

grade 2 - frequent PVCs, > 1/min or 30/hr

grade 3 - multiform PVCs

grade 4a - repetitive PVCs in couplets

grade 4b - ventricular tachycardia (VT)- ≥ 3 consecutive PVCs

grade 5 - early PVCs (R on T)

Conduction Disturbances

First-degree atrioventricular (AV) block - PR interval > 0.20 sec

Second-degree AV block

Type I (Wenckebach) - progressive lengthening of PR interval until a beat is dropped

Type II - series of non-conducted P waves

Third-degree (Complete) AV block - independent atrial and ventricular activity

Ventricular Conduction Disturbances (VCD) - Minnesota code VII[64] - Incomplete or Complete, Right (R), Left (L), or Indeterminate Bundle Branch Block (BBB)

Sinus Arrhythmia - irregular sinus rhythm with adjacent cycle lengths varying by ≥ 100%

Sinus Pause - > 1.75 sec

ST-T wave abnormalities

Significant ST-segment depression - > 1mm, measured at 0.08 sec from the J-point

Nonspecific ST-T wave changes - absent prominent R wave; ST-segment depression - > 1mm and/or primary T wave inversion or flattening

Significant Q waves - Minnesota code I-1, I-2 except I-2-h[64]

Left Ventricular Hypertrophy (LVH) - high amplitude R and S waves in chest leads, > 35 mm, or R wave > 13 mm in aVL, and major or minor ST-T abnormalities

Major ECG Abnormalities - LVH, VCD, ST-T wave abnormalities, VT, significant Q waves

Coronary Artery Disease Risk Factors

Data for CAD risk factors were collected on all subjects. Medical history questionnaires were completed by all subjects prior to exercise testing. Information concerning personal history of CAD, family history of coronary or other atherosclerotic disease in parents or siblings prior to age 55 yr,[65] smoking history and presence of diabetes mellitus were obtained. Classification for hypertension and blood lipid data followed standards given by the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure,[66] and National Cholesterol Education Program,[67] respectively. Standard 12-lead resting ECGs were assessed to determine pre-existing abnormalities related to CAD. Specific standards included:

Hypertension

Mild to Moderate:	Systolic BP	140-159 mm Hg
	Diastolic BP	90-114 mm Hg
Severe:	Systolic BP	≥ 160 mm Hg
	Diastolic BP	≥ 115 mm Hg

Hypercholesterolemia

Total Cholesterol		
	Borderline:	200-239 mg/dl
	Absolute:	≥ 240 mg/dl
Total Cholesterol:HDL Ratio		> 5
Obesity		> 25% fat

Diabetes mellitus

Fasting Glucose ≥ 140 mg/dl

Resting ECG Abnormalities

LVH, VCD, nonspecific ST-T wave changes, significant Q waves

Exercise Related Acute Cardiac Events

Exercise related acute cardiac events were defined as MI or SCD occurring within one hour of physical activity.

Radionuclide Angiography and Thallium Perfusion Studies

On Day 2 of T2, rest and exercise radionuclide angiography studies were performed in the afternoon, approximately 4 to 5 hr after treadmill exercise. These studies were made to further examine cardiac function and assist in determining the existence of overt heart disease. First pass radionuclide angiograms were obtained using a multicrystal gamma scintillation camera (Baird System 77). All studies were performed with the subjects seated upright on an electrically braked cycle ergometer (W.E. Collins) with the chest in the 30 degree right-anterior oblique position relative to the camera. The resting study was obtained immediately prior to exercise. Exercise began with a power output of 25 watts and pedal frequency of 60-70 rpm. The power output was increased 25 watts every 2 min until the subject could no longer continue. Exercise studies were made

during the last 30 sec of exercise at the peak power output obtained. Studies were examined by a cardiologist and classified as normal or abnormal.

Normal - left ventricular ejection fraction = 64% ± 14%, and no focal wall motion abnormalities;

Abnormal - focal wall motion abnormalities, or left ventricular ejection fraction < 50% or > 88%.

At T3 rest and exercise thallium perfusion scanning studies were performed to assess the presence of clinically silent ischemia. The exercise study was incorporated into the maximal treadmill exercise test on Day 1 using the Bruce protocol. During the last minute of exercise 2 mCi of ^{201}thallium was injected intravenously. Four to five minutes post exercise, images of thallium distributions were obtained using a three-headed rotating gamma camera (TRIONIX Company, TRIAD 88). The acquisition parameters of the 360° arc were: Step and shoot, 120° on each head, 40 stops at 3°/stop, 20 sec/stop, total acquisition time of 15 minutes. Rest studies were obtained 24 hours after exercise. The subject was reinjected with 1.5 mCi of ^{201}thallium and after 10 minutes redistribution/reinjection images were obtained with the same acquisition parameters. Rest and exercise studies were compared by a nuclear medicine physician and assessed positive or negative for ischemia.

Statistical Analysis

Physical characteristics, training data and blood values were compared using repeated measures analysis of variance. Data were analyzed to compare group and subgroup responses over three time periods T1, T2, and T3 (design:3 group x 3 time) When means were determined significantly different, contrast analyses were performed to determine which individual treatment means were significantly different. The nonparametric data obtained from ECG analyses, and CAD risk factor assessment were analyzed using the McNemar test, which is a repeated measures test for nominal variables.[68] Statistical significance was accepted as $p \leq 0.05$. Although some subjects changed subgroup status between the two follow-up periods, our choice of analysis (using status at T3) allows for a comparison between T1 vs T2, T1 vs T3, and T2 vs T3. The other alternative which assigned subjects to a subgroup based on status at 10-yr and 20-yr follow-up allowed only two comparisons, T1 vs T2, and T1 vs T3. This type of analysis could potentially ignore significant changes during the last 10-yr period and falsely imply that gradual changes occurred when in fact more abrupt changes occurred.

CHAPTER 4
RESULTS

Physical Characteristics

Physical characteristics at T1, T2, and T3 for the total group of subjects are compared in Table 1, and for the subjects divided by subgroups (H, M, L) in Table 2. At T3 subjects were 60- to 92-yr-old. Mean age of all subjects at T3 was 71.2 ± 8.8 yr and was similar for the three training subgroups, ranging from age 70.2- to 73.5-yr. Height significantly decreased ($p \leq 0.01$) between each evaluation for the total group. For the H subgroup height was significantly less ($p \leq 0.01$) at T3 compared to T1 and T2. For the M subgroup height significantly decreased ($p \leq 0.01$) from T1 to T2, and T1 to T3. For the L subgroup height was not significantly different.

For the total group body weight was similar at T1 and T2, but was significantly greater at T3 compared to T2 ($p \leq 0.05$). For the H and M subgroups weight remained similar, but the L subgroup significantly increased ($p \leq 0.05$) weight at T3 compared to T2. An interaction occurred with FFM for the total group. For the H and M subgroups FFM significantly decreased ($p \leq 0.01$) at T2 compared to T1, and T3 compared to

T1. For the L subgroup FFM was similar at T1 and T3, but at T2 FFM was significantly less ($p \leq 0.05$) than T1 and T3. Percent fat significantly increased ($p \leq 0.01$) for the total group, H subgroup, and M subgroup between all evaluations. For the L subgroup %fat was significantly greater ($p \leq 0.01$) at T3 than at T1 and T2.

Because one subject was using antihypertensive medication at T3 (Prinzide, Table 7), his data were not included in the analysis of resting BP measurements. In addition, data were not collected for resting HR for one subject (M subgroup, age 83 yr) under standard conditions at T1, and his data were not included the analysis of resting HR measurements.

Maximum oxygen uptake for the total group significantly decreased ($p \leq 0.01$) from T1 to T2, at a rate of approximately 9%/decade. At T3 VO_2max was significantly less ($p \leq 0.01$) than T1 and T2. The rate of decline from T2 to T3 was approximately 19%/decade, but the average rate over 20-yr was approximately 13%/decade. For the H subgroup VO_2max significantly decreased ($p \leq 0.05$) from T1 to T2, at a rate of approximately 7%/decade. At T3 VO_2max was significantly less ($p \leq 0.01$) than T1 and T2. The rate of decline from T2 to T3 was approximately 17%/decade, but the average rate over 20-yr was approximately 11%/decade. Maximum oxygen uptake declined significantly ($p \leq 0.01$) between all evaluations for the M subgroup. The rate of decline for the M subgroup was: T1 to T2 = approximately 8%/decade; T2 to T3 = approximately

17%/decade; average rate over 20-yr = approximately 12.5%/decade. Maximum oxygen uptake declined significantly ($p \leq 0.05$ T1 vs T2; $p \leq 0.01$ T1 vs T3, T2 vs T3) between all evaluations for the L subgroup. The rate of decline for the L subgroup was: T1 to T2 = approximately 17%/decade; T2 to T3 = approximately 35%/decade; average rate over 20-yr = approximately 27%/decade.

Maximum HR significantly declined ($p \leq 0.01$) at T2 and T3 compared to T1, at the rate of 5 to 8 beats/min per decade for the total group, and the H subgroup. For the M subgroup maximum HR significantly declined ($p \leq 0.01$) between all evaluations at the rate of 7 to 8 beats/min per decade. For the L subgroup maximum HR decreased insignificantly ($p > 0.05$), though T1 maximum HR was 6 to 3 beats/min greater than maximum HR at T2 and T3. Resting HR remained similar between T1 and T2, but was significantly higher at T3 (mean = 4 beats/min) than T1 ($p \leq 0.05$), and T2 ($p \leq 0.01$), for the total group. No significant differences in resting HR were found for the subgroups, though trends appeared in all groups for an increase in resting HR at T3.

Resting systolic and diastolic BP remained low, and did not significantly change for the total group and all subgroups.

Blood Lipids and Glucose Levels

Group and subgroup means of blood lipids and glucose levels at T1, T2, T3 are compared in Tables 3 and 4, respectively. HDL-cholesterol and glucose analyses were not performed at T1. At T2 HDL-cholesterol data for one subject (M subgroup, 63 yr), and glucose data for another subject (M subgroup, 71 yr) were not collected. Initially, total cholesterol levels for the total group (mean = 211 mg/dl), and H subgroup (mean = 234 mg/dl), were above current recommendations (< 200 mg/dl).[67] Total cholesterol levels decreased ($p \leq 0.01$) and were within CAD risk factor guidelines at T2 for both the total group and H subgroup. At T3 total cholesterol remained similar to T2 values for the total group and H subgroup. The total cholesterol:HDL-cholesterol ratio increased ($p \leq 0.01$), while HDL-cholesterol levels decreased ($p \leq 0.01$) for the total group at T3. However, the mean Total cholesterol:HDL-cholesterol ratio remained within CAD risk factor guidelines (< 5). A similar trend was observed with the subgroups, though only the decreases in HDL-cholesterol at T3 for the H and M subgroups were significantly different.

Mean values for glucose for the total group appear similar but an interaction occurred. Glucose levels remained similar for the H and M subgroups, but significantly

increased ($p \leq 0.05$) for the L subgroup. No subjects were initially or later became diabetic.

A comparison of 50th percentile age group norms[69] and mean values for athletes is shown in Table 5. No norms are presently available for subjects ≥ 90 yr of age. Data for the athletes show superior values for VO_2max, %fat, total cholesterol, total cholesterol:HDL-cholesterol ratio, maximum and resting heart rates, and resting systolic and diastolic blood pressure. Values for glucose levels and HDL-cholesterol appear relatively similar.

Training Data

Table 6 shows training data for subjects. Average training pace (min/mi) remained similar from T1 to T2 for all groups and subgroups. At T3 mean training pace for all subjects increased ($p \leq 0.01$) more than 2.5 min from T1, and increased ($p \leq 0.01$) slightly less than 2 min from T2. All subgroups significantly increased training pace at T3. The H subgroup's pace at T3 increased ($p \leq 0.01$) by > 1.5 min compared to T1, and increased ($p \leq 0.05$) by approximately 1.2 min compared to T2. The M subgroup's pace increased ($p \leq 0.01$) by 2.2 min at T3 compared to T1, and by > 1.3 min ($p \leq 0.01$) compared to T2. The highest increase in pace was in the L subgroup. Both subjects changed mode of exercise from running to walking. At T3 training pace had increased ($p \leq$

0.01) by 8.9 min compared to T1, and had increased ($p \leq 0.01$) 7.5 min from T2.

Weekly mileage decreased from T1 but was not significantly different until T3 for group and subgroup data. At T3 weekly mileage had decreased ($p \leq 0.01$) by 47% from T1, and was 32% less ($p \leq 0.05$) than T2 for the group. The H subgroup's weekly mileage at T3 decreased ($p \leq 0.01$) 43% compared to T1, and decreased ($p \leq 0.05$) 36% compared to T2. The M subgroup's weekly mileage decreased ($p \leq 0.05$) 48% at T3 compared to T1, and 27% compared to T2. Although no significant differences were obtained, the L subgroup's weekly mileage decreased 60% at T3 compared to T1, and 38% compared to T2.

Few subjects performed strength training initially and at T2 (1 and 2 subjects, respectively). At T3, however, 13 of 19 (68%) subjects ($p \leq 0.01$ T1 vs T3, T2 vs T3) had incorporated strength training into their fitness routines. The greatest increase ($p \leq 0.05$ T1 vs T3, T2 vs T3) was seen in the M subgroup. One subject cross-country skied during the winter months at T1, T2, and T3, while another subject was cross-country skiing at T2 and T3. At T3 one subject exercised regularly on a stationary cycle, primarily to reduce stress on his knees.

Medications and Health Problems

Table 7 shows use of medications and occurrence of common health problems encountered by the subjects. At T1 and T2 no subjects were regularly using medications. However, at T3, 11 of 19 (58%) were regularly using aspirin ($p \leq 0.01$ T1 vs T3, T2 vs T3), and use was greatest among the H subgroup (6 of 8 subjects, $p \leq 0.05$ T1 vs T3, T2 vs T3). Two subjects were using cardiovascular drugs at T3. One subject (L subgroup, age 75 yr) was on Prinzide (a combination of an angiotensin converting enzyme (ACE) inhibitor and diuretic) for treatment of hypertension. Another subject (M subgroup, age 61 yr) was using Flecainide to control paroxysmal atrial fibrillation.

No MI or SCD occurred during physical activity through the 20-yr follow-up period. No cardiovascular events occurred from T1 to T2. However, between T2 and T3, five subjects had cardiovascular problems requiring medical attention. Only one subject (M subgroup), at age 57 yr, experienced cardiovasular problems (paroxysmal atrial fibrillation) during physical activity (5K road race). Subsequent coronary artery catheterization was normal. Two subjects had episodes of transient ischemic attacks (TIAs; first subject at age 72 yr, H subgroup; second subject at age 64 yr, M subgroup). One subject (M subgroup), at age 87 yr, had a mild CVA. Another subject (M subgroup), at age 77 yr, had two episodes of

angina. This subject had one vessel CAD (by coronary artery catheterization) and underwent balloon angioplasty. All subjects recovered and are physically training.

Orthopedic problems that interfered with aerobic training included: back, hip, knee, foot and lower extremity soft tissue injuries. Few subjects (three) reported injuries at T1. At T2 > 50% ($p \leq 0.05$) of the subjects reported injuries. At T3, 15 of 19 subjects (79%) reported injuries ($p \leq 0.01$ T1 vs T3), and injuries were greatest in the H subgroup ($p \leq 0.05$ T1 vs T3).

An increase in the incidence of prostate problems was observed over 20-yr follow-up. At T1 the incidence was none, but increased to four subjects at T2, and six subjects at T3 ($p \leq 0.05$ T1 vs T3).

Occurrence of Arrhythmias and Electrocardiographic Abnormalities

Table 8 shows the occurrence of arrhythmias and ECG abnormalities during maximal treadmill exercise (GXT) and Holter monitoring (HM). The data in GXT-T2 and GXT-T3 represent values from treadmill exercise on Day 1 of testing with some exceptions discussed below. Data were analyzed for differences between Day 1 and Day 2, at T2 and T3. No significant differences were found between days except for VA grade 2, at T2. On Day 1 10 subjects had the arrhythmia, while on Day 2 one subject had the arrhythmia ($p \leq 0.01$). Because of the serious potential consequences of VT, data for

VT represent its occurrence in subjects for both Day 1 and Day 2, at T2 and T3. The data for incomplete LBBB and 2° AV block (Wenkebach) were observed only during Day 2 at T3. Two subjects were on cardiovascular medications (Prinzide, Flecainide, Table 7) at T3. Both subjects data were included in the analyses.

Maximal Treadmill Exercise

All subjects remained hemodynamically appropriate and asymptomatic during all testing. At T1 the occurrences of all arrhythmias and conduction disturbances were low except bradycardia. No subjects had complex VA (≥ grade 3) or ST-segment depression.

At T2 there was a significant increase ($p \leq 0.01$) in VA grade 1 (4 subjects = 21% vs 14 subjects = 74%), and VA grade 2 (2 subjects = 11% vs 10 subjects = 53%), though differences were not significant among subgroups. The occurrence of conduction disturbances was similar, and the occurrence of complex VA and ST-segment depression was low (2 subjects = 11%, per arrhythmia). Ventricular tachycardia occurred in one subject on Day 1, and a different subject on Day 2. ST-segment depression occurred in the same two subjects on both test days, but these subjects were different from those with VT.

At T3 the occurrence of PACs (11 subjects = 58%) significantly increased ($p \leq 0.05$) compared to T1 (4 subjects

= 21%), and was significantly higher in the H subgroup (1 vs 7 subjects, $p \leq 0.05$). At T3 there was a significant increase in VA grade 1 (4 subjects = 21% vs 14 subjects = 74%, $p \leq 0.01$), and VA grade 2 (2 subjects = 11% vs 9 subjects = 47%, $p \leq 0.05$), compared to T1, though differences were not significant among subgroups. No significant differences were observed in the occurrence of arrhythmias or ECG abnormalities between T2 and T3. At T3 the occurrence of complex VA remained low, but had slightly increased ($p > 0.05$). Ventricular tachycardia occurred in one subject on Day 1, and two different subjects on Day 2. One of these subjects also had complete LBBB at rest and during exercise (present on Day 1 and Day 2), and had 2° AV block (Wenkebach) during recovery, following VT. ST-segment depression occurred in the same two subjects on both test days, but these subjects were different from those with VT. At T2 and T3, the occurrence of VT in all subjects was at peak exercise or during the immediate post-exercise recovery period (≤ 5 min post-exercise). All occurrences of VT were nonsustained with runs ≤ 4 beats.

The occurrence of arrhythmias by age groups (at T3) are shown for those arrhythmias with significant changes (PACs, VA grade 1, and VA grade 2), in Figures 1, 2, and 3. Figure 1 shows the occurrence of PACs by age groups. This figure shows a trend in which subjects (except the oldest subject) have low initial incidences of the arrhythmia. As subjects age, incidences progressively increase at T2 and T3, but the older

groups have greater relative percentages. Figures 2 and 3 show the occurrence of VA grades 1 and 2, respectively, by age group. Both figures have a similar pattern in which there are low initial incidences of the arrhythmias in all but the oldest subject. At T2 there is an increase which is proportionally greater in the older age groups. At T3 incidences remained relatively similar among age groups.

Table 9 shows the prevalence of major ECG abnormalities by age groups. Certain major ECG abnormalities (LVH, nonspecific ST-T wave changes, significant Q waves) were never present. We observed that VT and VCD did not appear in subjects before age 60 yr. We also observed that major ECG abnormalities were persistent in subjects, as one subject who had ST-segment depression at T2 had ST-segment depression at T3, one subject who had VT at T2 had VT at T3, and one subject who had VCD at T1 had the abnormality at T2, and T3.

Table 10 shows major ECG abnormalities and use of cardiovascular medications. At T1 and T2 no medications were regularly used. At T3 the two subjects using cardiovascular medications had major ECG abnormalities which were not present in either subject at T1 or T2. At T3 the subject using Prinzide had ST-segment depression (present at Day 1 and Day 2). Another subject used Flecainide at T3. This subject had incomplete LBBB on Day 2 of testing but not Day 1. On inspection of the subject's medication record it was found that on Day 1 the subject postponed taking his medication until after exercise testing, while on Day 2 the

subject took his medication in the morning 4-5 hr prior to exercise testing.

Holter Monitoring

Holter monitoring was conducted for 19.3 ± 3.2 hr at T2, and 17.4 ± 1.3 hr at T3. No significant differences were observed between T2 and T3 (Table 8) for any arrhythmias or ECG abnormalities, which was similar to the pattern observed during treadmill exercise for T2 and T3. Because conditions and length of monitoring were dissimilar between treadmill exercise and Holter monitoring, no statistical analyses were performed. However, certain observations are noted. The absolute occurrence of PACs was greater during Holter monitoring compared to treadmill exercise (GXT-T2, n = 8 vs HM-T2, n = 14; GXT-T3, n = 11 vs HM-T3, n = 18). The occurrence of all VA was similar between treadmill exercise and Holter monitoring though no episodes of VT were observed during Holter monitoring. During Holter monitoring 1° AV block, incomplete RBBB (T2), and complete LBBB (T3) were observed, while incomplete LBBB, 2° AV block (Wenkebach), and ST-segment depression were not observed. The largest differences between treadmill exercise and Holter monitoring were in the occurrence of sinus arrhythmias (GXT-T2, n = 0, GXT-T3, n = 2 vs HM-T2, and HM-T3, n = 8), and sinus pauses (GXT-T2, and GXT-T3, n = 0 vs HM-T2, n = 5, HM-T3, n = 7), which were rare during treadmill exercise but frequent during

Holter monitoring. Except for two subjects, the sinus arrhythmias and sinus pauses occurred at night. Although the incidence of bradycardia was high at treadmill exercise (T1 = 94%, T2 = 94%, T3 = 78%), all subjects had bradycardia during Holter monitoring, primarily during the night.

Radionuclide Angiography and Thallium Perfusion Studies

At T2 all subjects had rest and exercise radionuclide angiography studies, and all studies were normal. At T3 rest and exercise thallium perfusion scans were performed. Thirteen of 19 studies were negative, and six studies were positive for ischemia. Of the six positive studies, only one was from a subject with major ECG abnormalities. This subject had complete LBBB, VT, and 2° AV block. Neither of the two subjects with ST-segment depression had positive thallium studies.

Changes in Coronary Artery Disease Risk Factors

Although no significant changes were found in the occurrence of CAD risk factors (Table 11), some trends toward a change in risk factors were found. The prevalence of any hypercholesterolemia decreased from 10 subjects (52%) to four (21%), from T1 to T3 (p = 0.11), and absolute hypercholesterolemia decreased from four subjects to 0 (p = 0.13), from T1 to T3. This positive trend, however, was countered by an increase in the number of subjects who had

total cholesterol:HDL-cholesterol ratios > 5 (T2 = two subjects (11%), T3 = six subjects (32%), $p = 0.13$).

There were slight changes (≤ 11%) observed in the prevalence of hypertension and resting ECG abnormalities. The overall incidence of any hypertension remained unchanged (4 subjects = 21%) but the incidence of absolute hypertension decreased from two subjects at T1 and T2, to none at T3. Resting ECG abnormalities were unchanged at T1 and T2 (1 subject = 5%), but increased slightly at T3 to three subjects (16%). Of the four categories of resting ECG abnormalities (LVH, VCD, nonspecific ST-T wave changes, significant Q waves), only incidences of VCD were observed. The prevalence of other risk factors showed no change (diabetes, smoking, obesity, family history of cardiovascular disease), and remained absent (diabetes, smoking, obesity), or low (family history of cardiovascular disease, 3 subjects = 16% at T1, T2, T3).

Table 1. Group Physical Characteristics

	Total Group		
	T1	T2	T3
n (subjects)	19	19	19
Age (yr)	51.3±8.6	61.0±8.9†	71.2±8.8††
Height (cm)	177.3±6.0	176.6±6.2†	175.8±6.5††
Weight (kg)	70.0±8.4	69.2±8.6	70.8±9.0¯*
FFM (kg)	61.2±6.3	58.8±6.2	58.5±6.6(In)
% Fat (Σ 7 Skinfolds)	12.2±4.2	14.7±4.2†	17.4±4.2††
VO2max (ml/kg*min)	54.2±8.4	49.4±7.4†	40.2±9.3††
Maximum Heart Rate (beats/min)	174±11	166±10†	161±9†
n (subjects)	18	18	18
Resting Heart Rate (beats/min)	48±7	48±8	52±8*†
Resting Systolic BP (mmHg)	121.0±17	123±15	124±13
Resting Diastolic BP (mmHg)	78±9	79±7	77±7

means±SD; T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); † p≤0.01 from T1; †† p≤0.01 T1 vs T3, T2 vs T3; *† p≤0.05 T1 vs T3, p≤0.01 T2 vs T3; ¯* p≤0.05 T2 vs T3; In (interaction between group and time); FFM (fat free mass); n (subjects) = 19 but not all subjects tested for all variables

Table 2. Subgroup Physical Characteristics

	High Intensity Group (H)			Moderate Intensity Group (M)			Low Intensity Group (L)		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
n (subjects)	8	8	8	9	9	9	2	2	2
Age (yr)	52.4±7.2	61.8±8.1†	71.8±8.1††	50.0±10.8	60.0±10.8†	70.2±10.7††	52.5±2.1	62.5±2.1†	73.5±2.0††
Height (cm)	174.8±5.4	174.7±5.7	173.4±6.1††	180.2±6.1	179.1±6.7†	178.4±6.8†	174.3±2.2	173.4±1.6	173.1±0.5
Weight (kg)	65.4±5.3	64.1±5.1	65.0±5.0	72.5±9.5	72.3±9.8	73.9±9.8	77.8±1.0	75.6±3.7	80.0±2.2¯*
FFM (kg)	58.4±4.1	55.7±3.7†	54.7±3.6†	63.1±7.8	60.9±7.7†	60.6±7.8†	63.9±0.6	61.6±1.9*	63.7±0.6¯*
% Fat (Σ 7 Skinfolds)	10.6±1.9	12.9±2.7†	15.8±2.5††	12.8±5.4	15.5±5.2†	17.8±5.1††	15.7±1.1	18.0±0.8	21.8±0.6††
VO2max (ml/kg*min)	55.3±9.3	51.7±7.8*	43.1±6.7††	54.1±8.2	49.2±6.9†	40.6±10.1††	50.0±8.7	41.6±2.3*	27.0±0.1††
Max HR (beats/min)	172±13	164±9†	159±10†	177±8	170±9†	162±10††	166±6	159±8	163±3
n (subjects)	8	8	8	8	8	8	2	2	2
R HR (beats/min)	46±7	47±10	50±11	51±8	49±7	54±6	50±3	48±11	56±8
n (subjects)	8	8	8	9	9	9	1	1	1
R Systolic BP (mmHg)	116±11	117±6	118±11	125±21	129±20	127±12	122±0	129±0	140±0
R Diastolic BP (mmHg)	76±7	79±8	74±6	80±10	79±7	79±6	78±0	84±0	90±0

means±SD; T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); R (resting); FFM (fat free mass);
* p≤0.05 from T1; † p≤0.01 from T1; †† p≤0.01 T1 vs T3, T2 vs T3; ¯* p≤0.05 T2 vs T3;
n (subjects) = 19 (8H,9M,2L) but not all subjects tested for all variables

Table 3. Group Blood Lipids and Glucose Means

	Total Group		
	T1	T2	T3
n (subjects)	19	19	19
Total Cholesterol (mg/dl)	211±36	183±34†	181±34†
n (subjects)	18	18	18
HDL-Cholesterol (mg/dl)	NA	56±15	44±10¯†
Total Cholesterol:HDL ratio	NA	3.5	4.3¯†
Glucose (mg/dl)	NA	101	102(In)

means±SD; T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); † p≤0.01 from T1; ¯† p≤0.01 T2 vs T3; NA (not available); In (interaction between group and time); n (subjects) = 19 but not all subjects tested for all variables

Table 4. Subgroup Blood Lipids and Glucose Means

	High Intensity (H)			Moderate Intensity (M)			Low Intensity (L)		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
n (subjects)	8	8	8	9	9	9	2	2	2
Total Cholesterol (mg/dl)	234±37	188±27†	188±33†	199±18	187±32	178±27	176±57	149±71	171±81
n (subjects)	8	8	8	8	8	8	2	2	2
HDL-Cholesterol (mg/dl)	NA	60.9±18.3	47.2±9.0¯†	NA	51.4±8.1	40.4±7.7¯*	NA	57.5±29.0	41.5±23.3
Total Cholesterol:HDL ratio	NA	3.5±1.8	4.1±0.9	NA	3.8±1.1	4.5±0.9	NA	2.6±0.1	4.2±0.4
Glucose (mg/dl)	NA	100±5	101±5	NA	102±6	100±4	NA	103±2	111±4¯*

means±SD; T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); † p≤0.01 from T1; ¯† p≤0.01 T2 vs T3; ¯* p≤0.05 T2 vs T3; NA (not available); n (subjects) = 19 (8H,9M,2L) but not all subjects tested for all variables

Table 5. Comparison of Athletes with Age Group Norms

Age Group (yr)	60-69				70-79				80-89				90+		
	Norm	n	Ath	n	Norm	n	Ath	n	Norm	n	Ath	n	Norm	Ath	n
%Fat (Skinfolds)	23.5	489	16.1	8	23.1	51	18.8	7	28.2	24	14.7	3	NA	25	1
VO2max (ml/kg*min)§	31.1	1402	48.3	8	28.0	203	34.6	7	29.6	43	37.9	3	NA	21.8	1
Total Cholesterol (mg/dl)	220	1251	193	8	215	171	181	7	204	40	157	3	NA	164	1
HDL-Cholesterol (mg/dl)	41	769	44	8	42	120	45	7	45	32	37	3	NA	32	1
Total Cholesterol:HDL	5.4	796	4.4	8	5.1	120	4.0	7	4.5	32	4.2	3	NA	5.1	1
Glucose (mg/dl)	104	1242	101	8	104	170	105	7	101	40	97	3	NA	101	1
Maximum HR (beats/min)	157	1402	161	8	142	203	163	7	140	46	159	3	NA	153	1
R HR (beats/min)	61	1413	50	8	62	207	56	7	62	47	46	3	NA	56	1
R Systolic BP (mmHg)	130	1415	122	8	138	208	127	7	130	48	117	3	NA	140	1
R Diastolic BP (mmHg)	82	1415	78	8	79	208	79	7	80	48	69	3	NA	78	1

§ (Norm values for VO2max estimated from performance time); n (subjects);
Ath (Athletes); NA (not available); R (resting);
Normative data reproduced with permission (courtesy of KH Cooper, S Blair, M Harris)[69]

Table 6. Training Data

	Total Group		
	T1	T2	T3
n	19	19	19
St Tr (≥2x per wk)	1	2	13††
CC Skiing	1	2	2
Cycling	0	0	1
Pace (min/mi)	8.00±1.29	8.73±1.50	10.64±3.20††
Miles (mi/wk)	35.0±23.9	27.8±15.5	18.8±11.9†*

T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up);
n (number of subjects); St Tr (strength training);
CC (cross country); means±SD; †† p≤0.01 T1 vs T3, T2 vs T3;
†* p≤0.01 T1 vs T3, p≤0.05 T2 vs T3

	High Intensity Group			Moderate Intensity Group			Low Intensity Group		
	T1	T2	T3	T1	T2	T3	T1	T2	T3
n	8	8	8	9	9	9	2	2	2
St Tr (≥2x per wk)	0	0	3	1	2	8**	0	0	1
CC Skiing	1	2	2	0	0	0	0	0	0
Cycling	0	0	0	0	0	1	0	0	0
Pace (min/mi)	8.19±1.24	8.59±1.30	9.78±1.07†*	7.97±1.50	8.85±1.88	10.17±3.58††	7.35±0.14	8.75±0.35	16.25±1.77††
Miles (mi/wk)	42.6±22.2	37.5±17.7	24.1±14.8†*	31.9±26.7	22.8±8.7	16.7±8.0*	18.8±5.3	12.0±4.2	7.5±.07

T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); n (number of subjects); St Tr (strength training);
CC (cross country); means±SD; * p≤0.05 from T1; ** p≤0.05 T1 vs T3, T2 vs T3;
†† p≤0.01 T1 vs T3, T2 vs T3; †* p≤0.01 T1 vs T3, p≤0.05 T2 vs T3

Table 7. Medications and Health Problems

	T1	T2	T3
	n	n	n
(Subgroup) Group	(8H,9M,2L) 19	(8H,9M,2L) 19	(8H,9M,2L) 19
Medication			
Aspirin	0	0	(6H**,3M,2L) 11††
Prinzide	0	0	(1L) 1
Flecainide	0	0	(1M) 1
Health Problem			
Cardiovascular	0	0	(1H,4M) 5
CAD	0	0	(1M) 1
Atrial Fibrillation	0	0	(1M) 1
TIA	0	0	(1H,1M) 2
CVA	0	0	(1M) 1
Orthopedic	(1H,2M) 3	(6H,3M,1L) 10*	(7H*,6M,1L) 15†
Prostate	0	(4H) 4	(3H,2M,1L) 6*

T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up);
n (subjects); H (high intensity group); M (moderate intensity group);
L (low intensity group); CAD (coronary artery disease);
TIA (transient ischemic attack); CVA (cerebral vascular accident);
* p≤0.05 from T1; † p≤0.01 from T1; ** p≤0.05 T1 vs T3, T2 vs T3;
†† p≤0.01 T1 vs T3, T2 vs T3

Table 8. Arrhythmias and Electrocardiographic Abnormalities

	GXT-T1	GXT-T2	GXT-T3	HM-T2	HM-T3
	n	n	n	n	n
(Subgroup) Group	(8H,9M,2L) 19	(8H,9M,2L) 19	(8H,9M,2L) 19	(8H,9M,2L) 19	(8H,9M,2L) 19
Premature Atrial Contractions	(1H,2M,1L) 4	(2H,5M,1L) 8	(7H*,3M,1L) 11*	(5H,7M,2L) 14	(8H,8M,2L) 18
Supraventricular Tachycardia	(1L) 1	0	(2H,1M) 3	(1M) 1	0
Atrial Flutter	0	0	(1H) 1	0	0
Ventricular Arrhythmias					
Grade 1 - occasional PVCs	(2H,2M) 4	(6H,6M,2L) 14†	(4H,8M,2L) 14†	(5H,7M,1L) 13	(5H,7M,2L) 14
Grade 2 - frequent PVCs	(2M) 2	(3H,7M) 10†	(3H,5M,1L) 9*	(2H,5M) 7	(2H,4M,1L) 7
Grade 3 - multiform PVCs	0	(2M) 2	(1H,1M,1L) 3	(4M) 4	(3M,1L) 4
Grade 4a - PVCs in couplets	0	(2M) 2	(1H,4M) 5	(1M) 1	(3M) 3
Grade 4b - VT	0	(2M) 2	(1H,2M) 3	0	0
1° AV Block	(2H,2M,1L) 5	(2H,2M,1L) 5	(3H,2M,1L) 6	(2H,2M,1L) 5	(2H,3M,1L) 6
2° AV Block (Wenckebach)	0	0	(1H) 1	0	0
Ventricular Conduction Defects					
Incomplete RBBB	(1H) 1	(1H) 1	(1H) 1	(1H) 1	0
Incomplete LBBB	0	0	(1M) 1	0	0
LBBB	0	0	(1H) 1	0	(1H) 1
Sinus Arrhythmia	0	0	(1H,1L) 2	(2H,4M,2M) 8	(3H,3M,2L) 8
Sinus Pause ≥ 1.75 sec	0	0	0	(2H,3M) 5	(3H,3M,1L) 7
Bradycardia (n=18 GXT)	(8H,7M,2L) 17	(7H,7M,2L) 17	(6H,7M,1L) 14	(8H,9M,2L) 19	(8H,9M,2L) 19
ST-Segment Depression	0	(1M,1L) 2	(2L) 2	0	0

GXT (maximal treadmill exercise); HM (Holter monitoring); T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); n (subjects); H (high intensity group); M (moderate intensity group); L (low intensity group); * $p \leq .05$ from T1; † $p \leq .01$ from T1; PVCs (premature ventricular contractions); AV (atrioventricular); RBBB and LBBB (right and left bundle branch block); VT (ventricular tachycardia); n (subjects) = 19 (8H,9M,2L) but not all subjects tested for all variables

Table 9. Major Electrocardiographic Abnormalities by Age

ST-Segment Depression						
Age(yr)	n	GXT-T1	GXT-T2	GXT-T3	HM-T2	HM-T3
60-69	(3H,5M)8	0	(1M)1	0	0	0
70-79	(3H,2M,2L)7	0	(1L)1	(2L)2	0	0
80-89	(2H,1M)3	0	0	0	0	0
90+	(1M)1	0	0	0	0	0
TOTAL	(8H,9M,2L)19	0	(1M,1L)2	(2L)2	0	0

Ventricular Tachycardia (Grade 4b)						
Age(yr)	n	GXT-T1	GXT-T2	GXT-T3	HM-T2	HM-T3
60-69	(3H,5M)8	0	0	(1H,1M)2	0	0
70-79	(3H,2M,2L)7	0	0	0	0	0
80-89	(2H,1M)3	0	(1M)1	0	0	0
90+	(1M)1	0	(1M)1	(1M)1	0	0
TOTAL	(8H,9M,2L)19	0	(2M)2	(1H,2M)3	0	0

Ventricular Conduction Defects						
Age(yr)	n	GXT-T1	GXT-T2	GXT-T3	HM-T2	HM-T3
60-69	(3H,5M)8	0	0	(1H,1M)2	0	(1H)1
70-79	(3H,2M,2L)7	0	0	0	0	0
80-89	(2H,1M)3	(1H)1	(1H)1	(1H)1	(1H)1	0
90+	(1M)1	0	0	0	0	0
TOTAL	(8H,9M,2L)19	(1H)1	(1H)1	(2H,1M)3	0	(1H)1

GXT (maximal treadmill exercise); HM (Holter monitoring);
n (number of subjects); T1,T2,T3 (initial evaluation,
10-yr follow-up, 20-yr follow-up); H (high intensity group);
M (moderate intensity group); L (low intensity group)

Table 10. Major Electrocardiographic Abnormalities and Medications

	T1			T2			T3		
		Medications			Medications			Medications	
ECG Abnormality	n	yes	no	n	yes	no	n	yes	no
ST-Segment Depression	0	0	0	2	0	2	2	1 (Prinzide)	1
Ventricular Tachycardia	0	0	0	2	0	2	3	0	3
Ventricular Conduction Defects	1	0	1	1	0	1	3	1	2
Incomplete RBBB	1	0	1	1	0	1	1	0	1
Incomplete LBBB	0	0	0	0	0	0	1	1 (Flecainide)	0
LBBB	0	0	0	0	0	0	1	0	1

T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); n (subjects); RBBB and LBBB (right and left bundle branch block)

Table 11. Changes in Coronary Artery Disease Risk Factors

	T1		T2		T3	
	n		n		n	
(Subgroup) Group	(8H,9M,2L)	19	(8H,9M,2L)	19	(8H,9M,2L)	19
Hypercholesterolemia	(6H,3M,1L)	10	(2H,4M)	6	(1H,2M,1L)	4
Absolute	(4H)	4	0		0	
Borderline	(2H,3M,1L)	6	(2H,4M)	6	(1H,2M,1L)	4
Total Cholesterol:HDL ratio > 5 (n=18)	NA		(1H,1M)	2	(2H,4M)	6
Hypertension	(1H,2M,1L)	4	(1H,2M,1L)	4	(3M,1L)	4
Severe	(1M,1L)	2	(1M,1L)	2	0	
Mild-Moderate	(1H,1M)	2	(1H,1M)	2	(3M,1L)	4
Diabetes mellitus	0		0		0	
Obesity	0		0		0	
Smoking	0		0		0	
Family History of CV Disease	(1H,2M)	3	(1H,2M)	3	(1H,2M)	3
Abnormal Resting ECG	(1H)	1	(1H)	1	(2H,1M)	3
Left Ventricular Hypertrophy	0		0		0	
Ventricular Conduction Defects	1		1		3	
Nonspecific ST-T Wave Changes	0		0		0	
Significant Q Waves	0		0		0	

T1,T2,T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up);
H (high intensity group); M (moderate intensity group); L (low intensity group);
n (subjects) = 19 (8H,9M,2L) but not all subjects tested for all variables;
CV (cardiovascular); NA (not available)

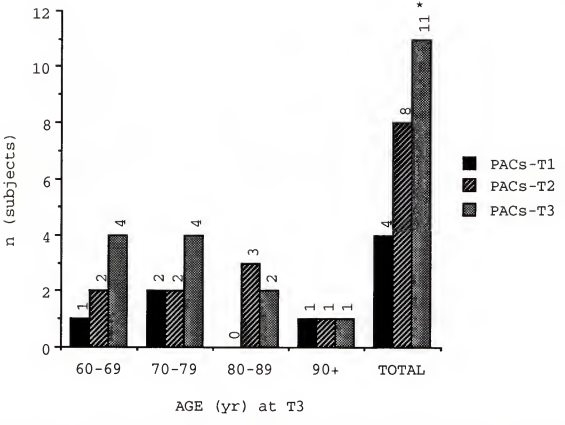

Figure 1. Occurrence of Premature Atrial Contractions (PACs) by Age Groups During Maximal Treadmill Exercise. T1, T2, T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); 60-69 yr age group n = 8; occurrence of PACs = 1, 2, 4 subjects at T1, T2, T3. 70-79 yr age group n = 7; occurrence of PACs = 2, 2, 4 subjects at T1, T2, T3. 80-89 yr age group n = 3; occurrence of PACs = 0, 3, 2 subjects at T1, T2, T3. 90+ yr age group n = 1; occurrence of PACs = 1, 1, 1 subject at T1, T2, T3. Total group n = 19; occurrence of PACs = 4, 8, 11* subjects at T1, T2, T3. * $p \leq 0.05$ from T1.

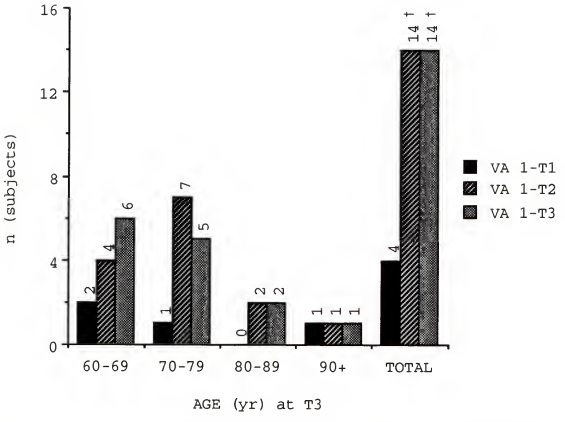

Figure 2. Occurrence of Grade 1 Ventricular Arrhythmias by Age Groups During Maximal Treadmill Exercise. VA 1 (Grade 1 Ventricular Arrhythmias); T1, T2, T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); 60-69 yr age group n = 8; occurrence of VA 1 = 2, 4, 6 subjects at T1, T2, T3. 70-79 yr age group n = 7; occurrence of VA 1 = 1, 7, 5 subjects at T1, T2, T3. 80-89 yr age group n = 3; occurrence of VA 1 = 0, 2, 2 subjects at T1, T2, T3. 90+ yr age group n = 1; occurrence of VA 1 = 1, 1, 1 subject at T1, T2, T3. Total group n = 19; occurrence of VA 1 = 4, 14†, 14† subjects at T1, T2, T3. † $p \leq 0.01$ from T1.

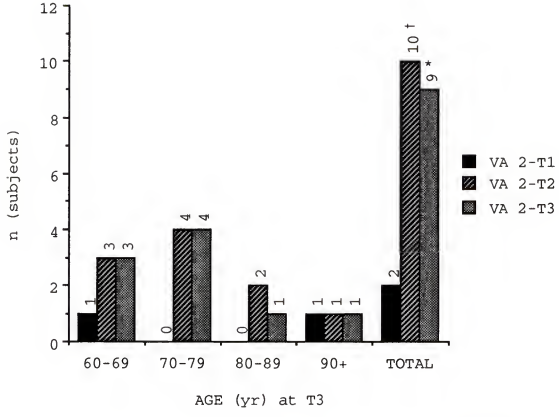

Figure 3. Occurrence of Grade 2 Ventricular Arrhythmias by Age Groups During Maximal Treadmill Exercise. VA 2 (Grade 2 Ventricular Arrhythmias); T1, T2, T3 (initial evaluation, 10-yr follow-up, 20-yr follow-up); 60-69 yr age group n = 8; occurrence of VA 2 = 1, 3, 3 subjects at T1, T2, T3. 70-79 yr age group n = 7; occurrence of VA 2 = 0, 4, 4 subjects at T1, T2, T3. 80-89 yr age group n = 3; occurrence of VA 2 = 0, 2, 1 subjects at T1, T2, T3. 90+ yr age group n = 1; occurrence of VA 2 = 1, 1, 1 subject at T1, T2, T3. Total group n = 19; occurrence of VA 2 = 2, 10†, 9* subjects at T1, T2, T3. † $p \leq 0.01$ from T1; * $p \leq 0.05$ from T1.

CHAPTER 5
DISCUSSION AND CONCLUSIONS

Discussion

Data concerning physical characteristics show these middle-aged and elderly athletes maintained superior condition in terms of aerobic capacity, body composition, blood lipids, maximum and resting HR, and resting BP through 20-yr follow-up. However, maximum HR, aerobic capacity, and body composition did significantly decline with age. The decline in maximum HR supports other data which have reported that regular aerobic training does not prevent the age-related decline in maximum HR, in healthy normal individuals, and athletes.[32,70] However, the present study suggests that the estimate for maximum HR based on the formula, 220 - age, underestimates the value for elderly athletes. For subjects age 70-79 yr, mean age was 74 yr, subjects age 80-89 yr, mean age was 81 yr, and one subject was age 92 yr. Estimated maximum HR values, for those respective groups, had errors (underestimates) of 10%, 13%, and 17% (see Table 5).

Significant decreases in training mileage and training speed were observed for most training groups at T3. A significant increase in orthopedic injuries occurred at T2

and T3. The injury incidence appears related to intensity of training as the high intensity group was the only subgroup with a significant increase in injuries.

The major questions asked in this study were as follows: Does habitual exercise and competition, in middle-aged and elderly athletes, alter the occurrence of cardiac arrhythmias, ECG abnormalities, and CAD risk factors? Does the occurrence of silent ischemic ST-segment depression and/or VT during maximal exercise testing predict increased risk for acute cardiac events during vigorous training and competition in this population? What are the acute cardiac risks associated with long-term vigorous training and competition in middle-aged and elderly athletes?

Age-Related Changes in Arrhythmias and Electrocardiographic Abnormalities

A significant increase in subjects with PACs at T3, and VA grades 1 and 2, at T2 and T3, was observed during GXT. As subjects aged, the prevalence of arrhythmias progressively increased at 20-yr follow-up for PACs (21% to 58%), and at 10-yr follow-up for VA grade 1 (21% to 74%), and VA grade 2 (11% to 53%). As the incidence of arrhythmias increased, the older age groups showed greater relative percentages. The occurrence of major ECG abnormalities (LVH, VCD, VT, ST-T wave abnormalities, and significant Q waves) remained low (0 to 16% per arrhythmia). We observed that VT and VCD were not present in subjects < 60 yr age, and major ECG abnormalities

persisted in 50% to 100% of those subjects with the abnormality, through follow-up. This study observed, throughout follow-up, lower incidences (0 to 11%) of ST-segment depression compared to cross-sectional studies, which reported incidences of approximately 20-25% in athletes, and physically active subjects.[25,39-40,54]

The use of medications by two subjects at T3 complicates the true nature of the prevalence of ECG abnormalities. Both subjects had major ECG abnormalities which were not present at T1 or T2. In one subject, on Prinzide, ST-segment depression was persistent during both days of testing. In the other subject, incomplete LBBB was observed only on Day 2 of testing. However, on Day 1 the subject had postponed taking his medication (Flecainide) until after exercise, whereas on Day 2 the subject took his medication before exercise. Thus, it is reasonable to suspect that medications may have been agents for the abnormalities in at least one of these subjects.

Since the incidence of arrhythmias was low initially, and all subjects were performing high intensity training and competition, another factor in the occurrence of arrhythmias, other than age, may be high intensity exercise. However, the data do not support this idea because the only subgroup which showed a significant increase in arrhythmias (PACs) was the high intensity group. In a cross-sectional study, Pilcher et al.[71] reported that the occurrence of arrhythmias was similar among runners (n = 80) who were divided into four groups

based on their training intensity. Together, these studies suggest training intensity is not an independent factor.

During HM no significant changes in the occurrence of arrhythmias and ECG abnormalities were observed between T2 and T3, which was similar to the occurrence of arrhythmias and ECG abnormalities during GXT. One can speculate that most changes probably occurred between T1 and T2, as was observed with GXT. The incidence of supraventricular arrhythmias was greater and VA similar during HM compared to GXT, but the occurrence of major ECG abnormalities was less during HM.

Only one other study (cross-sectional) has reported ECG data for master athletes during HM.[39] Northcote et al.[39] did not report the incidence of supraventricular arrhythmias but their study and the present study had similar incidences of VA (approximately 70 to 75%), sinus pauses (approximately 26 to 37% from T2 to T3 vs 40% from Northcote study), and 1° AV Block (26 to 32% from T2 to T3 vs 30% from Northcote study). However, this study observed lower incidences of 2° AV block (0 to 5%, T2 to T3), and 3° AV block (0%, T2 & T3), than reported from the Northcote study (2° AV block, 20%; 3° AV block, 15%).

Age-Related Changes in Coronary Artery Disease Risk Factors

An increase in CAD risk factors are associated with increased aged.[16-24] In this study, no significant changes were observed in the occurrence of risk factors. However, the

incidence of the most prevalent risk factor at T1 (hypercholesterolemia), showed a strong trend and decreased from 53% at T1, to 21% at T3. Mean values for total cholesterol significantly changed (decreased) at T2, but at T3 total cholesterol remained similar to T2 values. A decline in total cholesterol levels are reported for American men in general, from 1960 to 1980, and the decline has been associated with changes in diet.[67,72] However, the decline in this study is greater (T1 to T2 = 28 mg/dl, Table 3) compared to that reported for men age 65- to 74-yr (9 mg/dl).[72] The highest incidence of any single risk factor at T3, total cholesterol:HDL-cholesterol ratio > 5, was 32%. This increase was apparently caused by an age-related decline in HDL-cholesterol (which significantly declined at T3), because total cholesterol at T3 remained similar to T2 values.

The maintenance of resting BP throughout follow-up, without use of medication in 18 of 19 subjects, was unusual, as BP normally increases with age.[22-23] Among American men, age 65- to 74-yr, the incidence of hypertension has been estimated to be 59% to 67%.[22] Mean values (Tables 1 and 2) for systolic and diastolic BP remained similar, and the prevalence of any hypertension was the same (21%, Table 11) through follow-up. The prevalence of severe hypertension declined 11%, from two subjects at T1 and T2, to none at T3. However, this observation includes the one subject on antihypertensive medication. The lack of change in resting BP was likely due to exercise habits and weight control.[19,73-74]

In this study the incidences of abnormal resting ECGs were low (5 to 16%, T1 to T3), and lower than the incidences reported in the Cardiovascular Health Study, except for VCD which were similar.[17] Additionally, no subjects had LVH or significant Q waves, which are the strongest risk predictors of CAD, and SCD among the various resting ECG abnormalities.[16-17]

The occurrence of several risk factors did not change, and remained low, or were never present. No subjects smoked throughout follow-up which was expected due to the incompatibility of smoking and regular vigorous exercise. The prevalence of subjects with a family history of cardiovascular disease was low (16%), and did not change through follow-up. Mean glucose levels remained similar and no subjects had diabetes throughout follow-up. These data show a lower incidence of diabetes than have been reported in a large population study where the incidence of diabetes was approximately 17%, for males age 65- to 74-yr.[75] The results in this study support recent work that associates physical activity with decreased risk for NIDDM.[50]

Percent body fat significantly increased at each follow-up, but mean values remained much lower (approximately 26% lower at T3) than the general population,[69] and no subjects were obese. The group mean at T3 was 17% (mean age = 71 yr), which is the average value for men age 20- to 29-yr.[69]

Although other lifestyle factors, such as diet and weight control, may significantly influence CAD risk factors,

the observations in this study suggest that the overall prevalence of CAD risk factors were low, and that long-term moderate to vigorous exercise, in senior athletes, attenuates the increase in risk factors normally associated with aging.

Acute Risks of Cardiac Events During Strenuous Exercise, and Sensitivity of Exercise Testing in Predicting Acute Cardiac Events

The cumulative incidence of acute cardiac events (MI or SCD) during training and competition through 20-yr follow-up was 0%. These data include 5 of the 6 subjects not tested at T3, who were interviewed by telephone. The sixth subject may have had an acute cardiac event, though there was no death record in the county and state records, in his last known state of residence. These findings further support evidence from general population studies which show low risk for acute cardiac events during strenuous exercise.[4-8] No subjects at T1 had ST-segment depression or VT during GXT. At T2 two subjects had silent ST-segment depression, and two had nonsustained VT during GXT, though no subjects had both. Consequently, the sensitivity of ST-segment depression or VT during GXT, as markers for predicting acute cardiac events in senior athletes, during moderate to strenuous physical activity, is poor in this study (0/4 = 0%).

Our observations, however, are tempered by the fact that silent ST-segment depression or nonsustained VT may be sensitive (3 of 5 = 60%) for predicting increased overall

risk (during exercise and nonexercise periods) of cardiovascular complications (atrial fibrillation, TIA, CVA, CAD) in this population. We observed that one subject with silent ST-segment depression at T2, had acute atrial fibrillation during competition. Additionally, the two subjects with VT at T2, had cardiovascular problems (during nonexercise periods) between T2 and T3. One subject with VT had a mild CVA, and the other had angina and was found to have one vessel CAD (by coronary artery catheterization).

Summary

This study followed 19 senior athletes (mean age = 71 yr) who maintained regular aerobic training through 20-yr follow-up. We observed significant age-related changes in low grade arrhythmias (PACs, VA grades 1 and 2) during GXT, while the occurrence of major ECG abnormalities (ST-segment depression, VT, VCD) remained low or were never present (LVH, nonspecific ST-T wave changes, significant Q waves). We observed that VT and VCD were not present in subjects < 60 yr age, and major ECG abnormalities persisted through follow-up in 50% to 100% of those subjects with the ECG abnormalities. The appearance of arrhythmias did not appear related to training intensity. No incidence of acute cardiac events were recorded, and the risk of acute cardiac events during moderate to strenuous exercise and competition appears low in senior athletes. No significant changes in the occurrence of

CAD risk factors were observed and the overall prevalence of CAD risk factors remained low. These data suggest that habitual moderate to vigorous exercise, in senior athletes, attenuates the increase in CAD risk factors normally associated with aging.

Conclusions

With respect to senior athletes who have maintained long-term vigorous exercise and competition:

1) Changes in the occurrence of arrhythmias, in senior athletes, are few and primarily low grade.

2) Maximal exercise testing using silent ST-segment depression or nonsustained VT as clinical markers, has poor sensitivity in predicting risk for acute cardiac events during vigorous physical activity, in senior athletes.

3) The risk of acute cardiac events, in senior athletes, during moderate to strenuous physical activity is low.

4) Habitual vigorous physical activity attenuates the increase in CAD risk factors normally associated with aging.

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BIOGRAPHICAL SKETCH

Larry Jon Mengelkoch was born ten minutes before his identical twin brother, Jerry, on September 4, 1952, in Lafayette, IN. He was raised in Ohio and graduated from Yellow Springs High School (OH) in June, 1970.

He was honorably discharged from the U.S. Marine Corps in October, 1974. In June, 1978 he graduated from Ohio State University with a Bachelor of Science degree in zoology. He worked as a lab technician in water chemistry and insect chemistry laboratories before entering physical therapy school. In August, 1985 he graduated from the University of Florida with a Bachelor of Health Science degree in physical therapy. In January, 1986 he married Lourdes Maria Perez who was a classmate in physical therapy school. While working as a physical therapist he entered graduate school and completed the Master of Science degree in physical education at Florida International University in August, 1988. In August, 1989 he entered graduate school at the University of Florida to pursue the Doctor of Philosophy degree with a major in exercise and sport sciences and a minor in physiology. His degree program will be completed in August, 1992. Following graduation, he will pursue an academic career in a physical therapy curriculum.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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